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Enzyme with a memory for its substrate?

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In the interaction between an enzyme and its substrate, the enzyme is induced by the substrate followed by a change in enzymic conformation to fit the substrate. So far, many laboratories have been studying the neural memory. Recently, a few colleagues pay attention to enzymes involving the cellular storage of information [1], improving cellular memory and maintaining LTP [2]. Here, I would like to have a short discussion whether enzyme has a memory for the substrate after interaction with each other. As shown in Figure 1, *Eisenia fetida* protease I (*Ef*P-1) has at least two substrates (chromozym Th and chromozym U). *Ef*P-1 could not recognize chromozym U after reacted with chromozym Th. In contrast, the Km for chromozym Th became much greater after the enzyme had reacted with chromozym U [4]. In further investigation, *Eisenia fetida* protease II (*Ef*P-II) and subtilisin showed similar characteristics in the reaction with their substrates [5]. Lactate dehydrogenase (LDH) catalyzes the reversible reaction of pyruvate reduction to lactate. The affinity for lactate of LDH significantly became low after induced by pyruvic acid, and vice versa. This mnemonical-like characteristic is resulted from the conformational change in the interaction between the enzyme and substrate. S1 induces enzyme into a relatively stable complementary conformation that should not preferentially fit S2. It seems that the enzyme has got a memory for S1. Furthermore, if there are numbers (n) of S1, the enzyme memorizes the first molecule of S1 (n=1) in the interaction, then catalyzes the S1 one after another ($n \geqslant 2$) in a lock/key mechanism. Interestingly, wheat germ hexokinase LI has two initial states, X_1 being the form that binds glucose preferentially, and X_6 the one that binds glucose 6-phosphate. Meunier and colleagues [6] presented a theory that associates burst (or lag) kinetics with the respective concentrations of enzyme initial states X_1 and X_6 and with the cooperation of a mnemonical enzyme. It appears that the enzyme has acquired a memory for S1 after being induced by S1. How deep the memory is for S1 depends upon the stability of the conformation induced by S1. The yield of S1-induced enzyme will increase when S1 in-

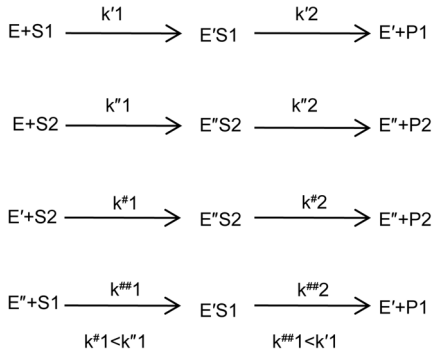

Figure 1 It is hypothesized that enzyme prefers S1 to S2 after the enzyme has reacted with S1. If an enzyme, for instance, an *Eisenia fetida* protease (called HbeAgase) [3] has at least two substrates (S1, chromozym Th and S2, chromozym U), the enzyme will be induced into different conformations to fit the substrates, respectively. Thus, there should be S1-induced conformation and S2-induced conformation of the enzyme. The enzyme with S1-induced conformation (E′), as if it has got a memory for S1, is complimentary to bind to S1, but not to S2, and vice versa, even though there is difference between the affinity of S1-induced enzyme to S2 and S2-induced enzyme to S1. E, enzyme; E′, enzyme with S1-induced conformation; E″, enzyme with S2-induced conformation; S1 and S2, substrate 1 and 2; P1 and P2, product 1 and 2.

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creases in cellular microenvironment. Resultantly, the cell has to express the nascent enzyme in response to the increase of S2, or S1-induced enzyme probably has its conformation changed through some cellular procedures to compensate the reaction with S2. The mnemonical characteristic for the substrate economizes the inducing procedure for another S1 ($n \geqslant 2$) when the enzyme is induced to fit S1 ($n=1$), decreases the transient free energy and improves the rate of enzymic catalysis.

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